therapeutic range, and the rate and extent of absorption are important to bioequivalence.

[42 FR 1635, Jan. 7, 1977. Redesignated and amended at 57 FR 18001, Apr. 28, 1992]

§ 320.34 Requirements for batch testing and certification by the Food and Drug Administration.

(a) If the Commissioner determines that individual batch testing by the Food and Drug Administration is necessary to assure that all batches of the same drug product meet an appropriate in vitro test, he shall include in the bioequivalence requirement a requirement for manufacturers to submit samples of each batch to the Food and Drug Administration and to withhold distribution of the batch until notified by the Food and Drug Administration that the batch may be introduced into interstate commerce.

(b) The Commissioner will ordinarily terminate a requirement for a manufacturer to submit samples for batch testing on a finding that the manufacturer has produced four consecutive batches that were tested by the Food and Drug Administration and found to meet the bioequivalence requirement, unless the public health requires that batch testing be extended to additional batches.

[42 FR 1635, Jan. 7, 1977. Redesignated at 57 FR 18001, Apr. 28, 1992]

§ 320.35 Requirements for in vitro testing of each batch.

If a bioequivalence requirement specifies a currently available in vitro test or an in vitro bioequivalence standard comparing the drug product to a reference standard, the manufacturer shall conduct the test on a sample of each batch of the drug product to assure batch-to-batch uniformity.

[42 FR 1635, Jan. 7, 1977. Redesignated at 57 FR 18001, Apr. 28, 1992]

§ 320.36 Requirements for maintenance of records of bioequivalence testing.

(a) All records of in vivo or in vitro tests conducted on any marketed batch of a drug product to assure that the product meets a bioequivalence requirement shall be maintained by the manufacturer for at least 2 years after the expiration date of the batch and submitted to the Food and Drug Administration on request.

(b) Any person who contracts with another party to conduct a bioequivalence study from which the data are intended to be submitted to FDA as part of an application submitted under part 314 of this chapter shall obtain from the person conducting the study sufficient accurate financial information to allow the submission of complete and accurate financial certifications or disclosure statements required under part 54 of this chapter and shall maintain that information and all records relating to the compensation given for that study and all other financial interest information required under part 54 of this chapter for 2 years after the date of approval of the application. The person maintaining these records shall, upon request for any properly authorized officer or employee of the Food and Drug Administration, at reasonable time, permit such officer or employee to have access to and copy and verify these records.

[42 FR 1635, Jan. 7, 1977. Redesignated at 57 FR 18001, Apr. 28, 1992, as amended at 63 FR 5252, Feb. 2, 1998]

§ 320.38 Retention of bioavailability samples.

(a) The applicant of an application or supplemental application submitted under section 505 of the Federal Food, Drug, and Cosmetic Act, or, if bioavailability testing was performed under contract, the contract research organization shall retain an appropriately identified reserve sample of the drug product for which the applicant is seeking approval (test article) and of the reference standard used to perform an in vivo bioavailability study in accordance with and for the studies described in paragraph (b) of this section that is representative of each sample of the test article and reference standard provided by the applicant for the testing.

(b) Reserve samples shall be retained for the following test articles and reference standards and for the studies described:

(1) If the formulation of the test article is the same as the formulation(s)

used in the clinical studies demonstrating substantial evidence of safety and effectiveness for the test article's claimed indications, a reserve sample of the test article used to conduct an in vivo bioavailability study comparing the test article to a reference oral solution, suspension, or injection.

(2) If the formulation of the test article differs from the formulation(s) used in the clinical studies demonstrating substantial evidence of safety and effectiveness for the test article's claimed indications, a reserve sample of the test article and of the reference standard used to conduct an in vivo bioequivalence study comparing the test article to the formulation(s) (reference standard) used in the clinical studies.

(3) For a new formulation, new dosage form, or a new salt or ester of an active drug ingredient or therapeutic moiety that has been approved for marketing, a reserve sample of the test article and of the reference standard used to conduct an in vivo bioequivalence study comparing the test article to a marketed product (reference standard) that contains the same active drug ingredient or therapeutic moiety.

(c) Each reserve sample shall consist of a sufficient quantity to permit FDA to perform five times all of the release tests required in the application or supplemental application.

(d) Each reserve sample shall be adequately identified so that the reserve sample can be positively identified as having come from the same sample as used in the specific bioavailability study.

(e) Each reserve sample shall be stored under conditions consistent with product labeling and in an area segregated from the area where testing is conducted and with access limited to authorized personnel. Each reserve sample shall be retained for a period of at least 5 years following the date on which the application or supplemental application is approved, or, if such application or supplemental application is not approved, at least 5 years following the date of completion of the bioavailability study in which the sample from which the reserve sample was obtained was used.

(f) Authorized FDA personnel will ordinarily collect reserve samples directly from the applicant or contract research organization at the storage site during a preapproval inspection. If authorized FDA personnel are unable to collect samples, FDA may require the applicant or contract research organization to submit the reserve samples to the place identified in the agency's request. If FDA has not collected or requested delivery of a reserve sample, or if FDA has not collected or requested delivery of any portion of a reserve sample, the applicant or contract research organization shall retain the sample or remaining sample for the 5-year period specified in paragraph (e) of this section.

(g) Upon release of the reserve samples to FDA, the applicant or contract research organization shall provide a written assurance that, to the best knowledge and belief of the individual executing the assurance, the reserve samples came from the same samples as used in the specific bioavailability or bioequivalence study identified by the agency. The assurance shall be executed by an individual authorized to act for the applicant or contract research organization in releasing the reserve samples to FDA.

(h) A contract research organization may contract with an appropriate, independent third party to provide storage of reserve samples provided that the sponsor of the study has been notified in writing of the name and address of the facility at which the reserve samples will be stored.

(i) If a contract research organization conducting a bioavailability or bioequivalence study that requires reserve sample retention under this section or § 320.63 goes out of business, it shall transfer its reserve samples to an appropriate, independent third party, and shall notify in writing the sponsor of the study of the transfer and provide the study sponsor with the name and address of the facility to which the reserve samples have been transferred.

[58 FR 25927, Apr. 28, 1993, as amended at 64 FR 402, Jan. 5, 1999]